U. S. ARMY MEDICAL RESEARCH & NUTRITION LABORATORY

PHYSIOLOGICAL AND BIOCHEMICAL EVALUATION OF POTENTIAL ANTI-FATIGUE DRUGS III THE EFFECT OF OCTACOSANOL, WHEAT GERM OIL AND VITAMIN E ON THE PERFORMANCE OF SWIMMING RATS

REPORT 275
11 MARCH 1963

UNITED STATES ARMY
MEDICAL RESEARCH AND DEVELOPMENT COMMAND

US ARMY MEDICAL RESEARCH AND NUTRITION LABORATORY
Fitzsimons General Hospital
Denver 30, Colorado

Report No. 275

11 March 1963

Report on

PHYSIOLOGICAL AND BIOCHEMICAL EVALUATION OF POTENTIAL ANTI-FATIGUE DRUGS. III. THE EFFECT OF OCTACOSANOL, WHEAT GERM OIL AND VITAMIN E ON THE PERFORMANCE OF SWIMMING RATS

By

C. Frank Consolazio
LeRoy O. Matoush
Richard A. Nelson
Gerhard J. Isaac
Laurence M. Hursh

Report No. 275
Project No. 3A012501A803 - Military Internal Medicine
Task No. 04: Pharmacology of the Combat Soldier
USAMRNL Sub-Task No.: 1-9d

11 March 1963

PHYSIOLOGICAL AND BIOCHEMICAL EVALUATION OF POTENTIAL ANTI-FATIGUE DRUGS. III. THE EFFECT OF OCTACOSANOL, WHEAT GERM OIL AND VITAMIN E ON THE PERFORMANCE OF SWIMMING RATS

OBJECT:

The object of this study was to evaluate the effects of the oral ingestion of octacosanol, wheat germ oil and vitamin E on the performance of swimming rats, using a single and double swim-to-exhaustion.

SUMMARY:

Two long term studies (6 weeks) were performed to evaluate the effects of octacosanol, wheat germ oil and vitamin E on the performance of swimming rats. In the first study the rats performed a single swim-to-exhaustion, two days a week, and in the second study a double swim-to-exhaustion was utilized two days a week.

Comparisons made during the study showed that the performance of rats receiving these substances did not differ significantly from that of control groups. These results are contrary to published data in the literature showing increases in performance with the various treatments.

APPROVED:

Marion E. McDowell

MARION E. McDOWELL
Lt. Colonel, MC
Director.

PHYSIOLOGICAL AND BIOCHEMICAL EVALUATION OF POTENTIAL ANTI-FATIGUE DRUGS. III. THE EFFECT OF OCTACOSANOL, WHEAT GERM OIL AND VITAMIN E ON THE PERFORMANCE OF SWIMMING RATS

Introduction

For many years the military forces have been interested in acquiring a non-toxic, non-habit forming substance for delaying the onset of fatigue, that would result in increasing performance and endurance in men. At the present time many so-called "anti-fatigue drugs" are available on the market, including substances such as octacosanol, wheat germ oil and vitamin E. These substances sometimes sold as "cure-alls" for improving mental and physical fatigue, stress, etc.

Since 1952 various experiments have been carried out at the University of Illinois Physical Fitness Research Laboratory concerning the value of wheat germ oil as an ergogenic aid for men trying to improve their physical fitness through regular exercise. The first published reports of this work appeared in October 1954 (1); further elaboration appeared in reports published in December 1954 (2), March 1955 (3), and December 1955 (4). Studies were also conducted in the Department of Biochemistry and Nutrition at the University of Southern California. The results of these studies were published in March 1955 (5).

A thorough review of the work done at the University of Illinois appears in their most recent publication (4). This review cites data which shows that the subjects taking the wheat germ oil supplement made greater gains in a number of physical fitness measurements than the subjects taking vitamin E, a placebo, or exercise alone.

Studies done on athletic teams failed to produce any conclusive data in favor of wheat germ oil. This lack of improvement was attributed to "competitive fatigue". It was concluded that the competitive sports studied, wrestling and swimming, are not suitable to show the effects of a dietary supplement.

The work done at the University of California produced results favoring diets containing wheat germ oil for prolonging the time it took guinea pigs to swim to exhaustion. In contrast to these findings rats fed a diet containing a wheat germ oil supplement did not swim longer than rats fed diets containing corn oil.

Although most of the data presented are in favor of wheat germ oil as an ergogenic aid, the failure of wheat germ oil to produce significant favorable results with athletic teams in competition or with rats in swimming tests, creates some doubt as to its usefulness. Recently it has been speculated that octacosanol was the factor in the wheat germ oil that

prolonged the onset of fatigue and aided endurance (6). Octacosanol-1 is an alcohol (octacosyl alcohol, $CH_3[CH_2]_{26}.CHOH$) with a molecular weight of 410 and a M.P. between 83.2 - 83.4°C. Percival (7), in his review of the literature on vitamin E and performance, has stated that alpha tocopheral (a) reduces the oxygen requirements of tissues, (b) improves the collateral circulation, (c) is a vasodilator, and (d) stimulates muscle power. To test the anti-fatigue effects of wheat germ oil, vitamin E and octacosanol, two experiments were designed on swimming rats, using a single and a double swim-to-exhaustion as a criteria of performance.

Experimental Design

In both experiments the swimming was done in large glass jars, 12 inches in diameter and 24 inches deep. The water level was maintained at 18 inches so that the rats could not get support from their tails touching the bottom of the jar and the margin at the top was enough so that the rats could not climb out. To keep the water mixed so that the temperature was uniform and to provide turbulence that served to keep the rats from floating, compressed air at the rate of 2 liters/minute was forced through a 2¼" O.D. glass tube placed down one side of the jars. The water temperature was maintained at 25°C. The rats swam in individual jars.

The first experiment was a single swim test using 60 Sprague-Dawley male rats. The rats were randomly assigned to three experimental groups. Group I (control) received no therapy at any time. Group II received 37.5 units of vitamin E, and Group III 6 minims of wheat germ oil. Therapy was administered for 5 weeks, followed by an additional recovery week without therapy. Therapy was administered orally, by stomach tube, for 5 days each week. In all instances this was done 30 minutes prior to the swimming.

In this experiment each rat was forced to swim to exhaustion on two days each week. The animals in each group were randomly divided into equal sub-groups. One sub-group of each group swam on Tuesdays and Thursdays and the other on Wednesdays and Fridays. The time recorded was for the period between the time the rat was placed in the water and the time it appeared that the animal was unable to continue to swim. A 9 gm weight was hung around the neck of each animal to provide an additional burden and to cut down on the swimming time.

The second experiment was a double swim test also using Sprague-Dawley rats. The 36 rats (18 males and 18 females) were randomly assigned to three experimental groups of 12 each, equally divided between males and females. The supplements came in 36 numbered vials, 12 each of a control oil, wheat germ oil, and octacosanol. Administration was by number and the code was not made known to the men carrying out the swim tests. Therapy was administered orally at the rate of 0.1 ml/day each afternoon during the therapy period. The three supplements, which were all the same color,

consisted of (a) a placebo oil made up of 92 parts of Wesson oil and 8 parts of soy lecithin, (b) a wheat germ oil containing 1.0 I.U. of vitamin E/0.1 ml, and (c) octacosanol in the placebo oil at a concentration of 0.11%. The experiment was divided into three periods, (a) week one, control, no therapy, (b) weeks 2 to 5, therapy, and (c) week 6, control or recovery, no therapy. The male rats carried a 10 gm weight and the females a 6.5 gm weight (approximately 3% of body weight) to provide an additional burden and to cut down on the swimming time.

The male rats swam on Monday and Thursday of each week and the female rats swam on Tuesday and Friday. The second swim of the day for each rat was always started 2½ hours after the end of its first swim.

Results

Average swimming times in the single swim experiment are shown in Table I. Sub-groups were combined to show averages for the first swim each week and for the second swim each week. Swims 1, 7 and 11 were selected for statistical analysis (Table II). The differences between the averages for the vitamin E and control groups were not statistically significant for any of these swims. This was also true for wheat germ oil and control groups for swims 1 and 7, but for swim 11, one week after therapy, the average for the wheat germ oil group was significantly lower ($P < 0.50$) than for control. Body weights in all groups increased slightly during the study (Table III).

Average swimming times in the double swim experiment are shown in Tables IV and V. Statistical analysis was performed on the data for the second swim day of each week. The differences between the averages for the octacosanol and wheat germ oil groups and the control group were not statistically significant except that in week 4, second swim, males, the average for the wheat germ oil group was lower than for control group, with a difference that was just barely significant at the 5% level.

Average body weights for all groups are shown in Table VI. No changes of importance appeared.

Table VII shows a simple count of the number of times the recorded time for a rat's swim 1 or swim 2 was the larger. The differences between therapy groups in the distribution of swims into such categories were not significant.

Discussion

Cureton and Pohndorf (4) working with humans have reported beneficial effects of wheat germ oil in increasing performance. Ershoff and Levin (5) have also shown the beneficial effects of wheat germ oil in increasing the

swimming time of guinea pigs but also observed that weanling rats fed wheat germ oil did not increase their swimming time when they were compared to rats fed corn oil. In the present study, it was observed that a wheat germ oil treated group did not improve significantly over a control group, in fact, during the recovery or final control period, the group who had received wheat germ oil swam for significantly less time than the controls.

As mentioned previously Percival (7) has reported the beneficial effects of vitamin E therapy, observing a decrease in the recovery pulses of men after completing an exhausting step test and after a 440 yard run. On the other hand Ershoff and Levin (5) in their guinea pig study showed that the addition of alpha tocopheral in the diet did not significantly change the performance of these animals. In the present study it was observed that the rats receiving the vitamin E therapy did not significantly increase their performance, when they were compared to a control group.

Under the conditions of the present study it could not be established that the administration to rats of wheat germ oil, vitamin E, or octacosanol improved performance. Measured by swim-time-to-exhaustion, whether single or double swims were utilized, the performance of rats receiving therapy was not significantly different from that of the controls. These findings are contrary to data reported in the literature, where increases in endurance have been observed after administration of substances such as wheat germ oil, vitamin E and octacosanol.

ACKNOWLEDGEMENTS

We especially wish to thank Mr. Billy J. James, SSG Juan B. Torres, SP5 Oktawian Tarnowieckyi, SP5 Lynn J. Maland, SP5 Gary L. Beal, SP4 Lester E. Jones, SP4 Warren E. Hendricks and SP4 Samuel D. Wilkins for their very valuable technical assistance in this study.

LITERATURE CITED

1. Cureton, T. K.: Exercise, wheat germ oil for middle aged men. Science News Letter 66: 216, 1954.

2. Cureton, T. K.: Effects of wheat germ oil and vitamin E on normal human subjects in physical training programs. Am. J. Physiol. (Abstract) 179: 628, 1954

3. Cureton, T. K.: Wheat germ oil, the wonder fuel. Scholastic Coach, 24: 36-37, 67-68, 1955.

4. Cureton, T. K. and Pohndorf, R. H.: Influence of wheat germ oil as a dietary supplement in a program of conditioning exercises with middleaged subjects. Res. Quart. 26: 391-407, 1955.

5. Ershoff, B. H. and Levin, E.: Beneficial effects of an unidentified factor in wheat germ oil on the swimming performance of guinea pigs. Fed. Proc. 14: 431-432, 1955.

6. Levin E.: Personal communication.

7. Percival, L.: Vitamin E in athletic efficiency. Preliminary Report, Shute Foundation for Medical Research 3: No. 2, December 1951.

TABLE I

Experiment 1: Swimming Times of Rats,

Means and Standard Deviations,

By Treatment and Swim Day

(In Minutes)

Swim Day	Treatment*					
	Control		Vitamin E		Wheat Germ Oil	
Therapy	Mean	± S.D.	Mean	± S.D.	Mean	± S.D.
1	15.6	9.8	13.7	6.2	10.9	7.5
2	17.8	8.4	15.7	7.2	12.0	4.2
3	25.7	19.9	22.4	11.1	18.8	11.2
4	30.3	24.5	23.1	18.0	24.3	29.4
5	33.8	21.8	30.4	26.8	23.8	17.6
6	23.0	10.3	24.5	20.8	32.2	30.1
7	24.9	12.1	35.1	22.4	29.4	25.7
8	32.9	29.2	22.0	4.8	22.7	10.5
9	30.7	17.2	30.3	21.7	39.6	38.9
10	28.8	16.1	31.7	16.9	23.2	10.4
Post-Therapy						
11	38.9	27.9	57.7	49.7	20.6	7.5
12	23.4	7.4	28.5	14.3	18.2	5.4

* Twenty male rats in each group. Single swim to exhaustion, twice a week.

TABLE II

Experiment 1: Swimming Time of Rats,

Means and Standard Deviations,

By Treatments and Selected Swim Days

(In Minutes)

Treatment	Swim 1 Mean	± S.D.	Swim 7 Mean	± S.D.	Swim 11 (No Therapy) Mean	± S.D.
Control	15.6	9.77	24.9	12.1	38.9*	27.9
Vitamin E	13.7	6.22	35.1	22.4	57.7	49.7
Wheat Germ Oil	10.9	7.48	29.4	25.7	20.6*	7.5

*Difference between control and wheat germ oil means significant ($P < .050$); all other comparisons between control and therapy groups are non-significant.

TABLE III

Experiment 1: Mean Body Weights,
Inital and at End of Each Week,
(In Grams)

Week of Therapy	Treatment		
	Control	Vitamin E	Wheat Germ Oil
Initial	337	335	351
Week 1	340	347	353
2	342	340	351
3	336	352	357
4	346	351	361
5	346	343	363
Post-Therapy			
6	347	349	376
Weight Change	+10	+14	+25

* Twenty male rats in each group.

TABLE IV

Experiment 2: Swimming Time of Male Rats,

By Treatment and Swim Day

(In Minutes)

	Swim Day 1		Swim Day 2			
Week of Treatment	Swim 1	Swim 2	Swim 1		Swim 2	
Control Oil	Mean	Mean	Mean	± S.D.	Mean	± S.D.
1	10.2	53.6	15.7	6.4	15.3	7.5
2	15.1	39.8	15.3	3.0	39.3	34.2
3	17.3	22.2	23.9	11.1	26.7	14.9
4	16.1	14.9	12.7	4.4	31.2	10.8
5	32.2	31.7	17.0	8.0	32.9	23.4
6	15.1	27.3	13.7	4.1	40.9	53.8
Octacosanol						
1	18.6	33.9	15.6	9.4	20.4	10.7
2	25.4	9.9	29.2	18.0	16.2	8.3
3	15.4	20.2	18.2	6.5	17.7	11.9
4	16.4	16.6	16.5	6.3	21.8	11.8
5	13.0	23.5	20.5	10.6	21.7	15.1
6	15.2	16.6	20.0	7.5	14.9	5.2
Wheat Germ Oil						
1	16.7	12.4	28.8	22.8	18.9	11.8
2	17.1	18.9	14.9	11.7	21.7	7.5
3	15.6	11.7	15.0	6.4	19.7	7.0
4	16.2	38.6	11.7	5.6	18.7	6.4
5	20.5	26.0	72.6	116.9	37.6	48.3
6	37.6	65.4	44.5	47.0	115.0	27.1

TABLE V

Experiment 2: Swimming Time of Female Rats

By Treatment and Swim Day

(In Minutes)

	Swim Day 1		Swim Day 2			
Week of Treatment	Swim 1	Swim 2	Swim 1		Swim 2	
Control Oil	Mean	Mean	Mean	± S.D.	Mean	± S.D.
1	13.7	16.1	14.9	2.9	13.9	6.3
2	12.8	14.0	15.7	6.2	13.1	4.7
3	12.9	12.8	13.5	3.2	11.6	3.5
4	10.0	12.6	12.1	2.6	11.1	2.7
5	11.1	13.5	19.8	8.6	17.5	8.3
6	9.4	20.2	12.9	5.6	32.7	42.5
Octacosanol						
1	16.1	13.9	11.8	3.4	13.3	4.2
2	14.1	11.2	25.5	35.3	12.1	4.9
3	14.9	11.2	13.1	4.4	11.9	2.1
4	15.2	26.7	10.5	2.5	17.3	7.3
5	14.3	26.7	16.8	6.5	52.1	35.7
6	14.4	36.6	28.7	21.7	14.3	4.5
Wheat Germ Oil						
1	43.9	12.8	15.4	13.2	11.3	3.6
2	20.6	15.1	30.4	41.5	13.7	6.3
3	15.4	37.8	12.4	2.3	19.8	13.1
4	12.0	13.8	16.1	4.8	10.8	3.9
5	15.2	16.0	19.6	9.8	30.1	31.7
6	13.4	30.0	27.5	27.6	22.6	15.7

TABLE VI

Experiment 2: Mean Body Weights, By Sex, Treatment and Week of Experiment*

(In Grams)

Week of Study	Control Oil	Wheat Germ Oil	Octaco-sanol	Control Oil	Wheat Germ Oil	Octaco-sanol
1	351	349	345	229	226	228
2	347	342	353	231	228	231
3	338	353	368	234	235	238
4	322	346	353	238	230	232
5	312	349	346	237	234	232
6	300	328	348	237	233	231

* Mean weights for 6 rats in each group.

TABLE VII

Experiment 2: Number of Times Swim 1 or Swim 2
Of a Given Swim Day Was the Longer,
By Treatment and Sex

Group		Control Oil	Wheat Germ Oil	Octacosanol
Males:	Swim 1	24	29	39
	Swim 2	41	38	33
Females:	Swim 1	28	37	28
	Swim 2	34	35	42
Combined:	Swim 1	52	66	67
	Swim 2	75	73	75

USA Medical Research & Nutrition Laboratory Proj #3A012501A803 Report #275

PHYSIOLOGICAL AND BIOCHEMICAL EVALUATION OF POTENTIAL ANTI-FATIGUE DRUGS. III. THE EFFECT OF OCTACOSANOL, WHEAT GERM OIL AND VITAMIN E ON THE PERFORMANCE OF SWIMMING RATS

C. Frank Consolazio, Le Roy O. Matoush, Richard A. Nelson
Gerhard J. Isaac and Laurence M. Hursh

12 pps, 7 Tables 11 March 1963 UNCLASSIFIED

Two separate swim-to-exhaustion experiments, using a single and a double swim, were performed to evaluate the effects of administering octacosanol, wheat germ oil and vitamin E, as a means of increasing endurance in rats. In both experiments, the swimming times of rats receiving therapy did not differ significantly from those for control animals

1. Performance
2. Anti-Fatigue Drugs
3. Swimming Tests
4. Octacosanol
5. Wheat Germ Oil
6. Vitamin E

USA Medical Research & Nutrition Laboratory Proj #3A012501A803 Report #275

PHYSIOLOGICAL AND BIOCHEMICAL EVALUATION OF POTENTIAL ANTI-FATIGUE DRUGS. III. THE EFFECT OF OCTACOSANOL, WHEAT GERM OIL AND VITAMIN E ON THE PERFORMANCE OF SWIMMING RATS

C. Frank Consolazio, Le Roy O. Matoush, Richard A. Nelson
Gerhard J. Isaac and Laurence M. Hursh

12 pps, 7 Tables 11 March 1963 UNCLASSIFIED

Two separate swim-to-exhaustion experiments, using a single and a double swim, were performed to evaluate the effects of administering octacosanol, wheat germ oil and vitamin E, as a means of increasing endurance in rats. In both experiments, the swimming times of rats receiving therapy did not differ significantly from those for control animals

1. Performance
2. Anti-Fatigue Drugs
3. Swimming Tests
4. Octacosanol
5. Wheat Germ Oil
6. Vitamin E

USA Medical Research & Nutrition Laboratory Proj #3A012501A803 Report #275

PHYSIOLOGICAL AND BIOCHEMICAL EVALUATION OF POTENTIAL ANTI-FATIGUE DRUGS. III. THE EFFECT OF OCTACOSANOL, WHEAT GERM OIL AND VITAMIN E ON THE PERFORMANCE OF SWIMMING RATS

C. Frank Consolazio, Le Roy O. Matoush, Richard A. Nelson
Gerhard J. Isaac and Laurence M. Hursh

12 pps, 7 Tables 11 March 1963 UNCLASSIFIED

Two separate swim-to-exhaustion experiments, using a single and a double swim, were performed to evaluate the effects of administering octacosanol, wheat germ oil and vitamin E, as a means of increasing endurance in rats. In both experiments, the swimming times of rats receiving therapy did not differ significantly from those for control animals

1. Performance
2. Anti-Fatigue Drugs
3. Swimming Tests
4. Octacosanol
5. Wheat Germ Oil
6. Vitamin E

USA Medical Research & Nutrition Laboratory Proj #3A012501A803 Report #275

PHYSIOLOGICAL AND BIOCHEMICAL EVALUATION OF POTENTIAL ANTI-FATIGUE DRUGS. III. THE EFFECT OF OCTACOSANOL, WHEAT GERM OIL AND VITAMIN E ON THE PERFORMANCE OF SWIMMING RATS

C. Frank Consolazio, Le Roy O. Matoush, Richard A. Nelson
Gerhard J. Isaac and Laurence M. Hursh

12 pps, 7 Tables 11 March 1963 UNCLASSIFIED

Two separate swim-to-exhaustion experiments, using a single and a double swim, were performed to evaluate the effects of administering octacosanol, wheat germ oil and vitamin E, as a means of increasing endurance in rats. In both experiments, the swimming times of rats receiving therapy did not differ significantly from those for control animals

1. Performance
2. Anti-Fatigue Drugs
3. Swimming Tests
4. Octacosanol
5. Wheat Germ Oil
6. Vitamin E